100

DISPLAY

104 — MODEL CONSTRUCTION WINDOW	EQUATIONS WINDOW — 108
112 — DEBUGGING WINDOW	MESSAGES WINDOW — 116

120

124 — GRAPHICAL USER INTERFACE

132

DEFINED BLOCKS

PROGRAM BLOCKS

136

144 — SIMULATION INTERPRETER

128 — EQUATIONS GENERATOR

152 — UNITS TRACKER

148 — MODEL LIBRARY
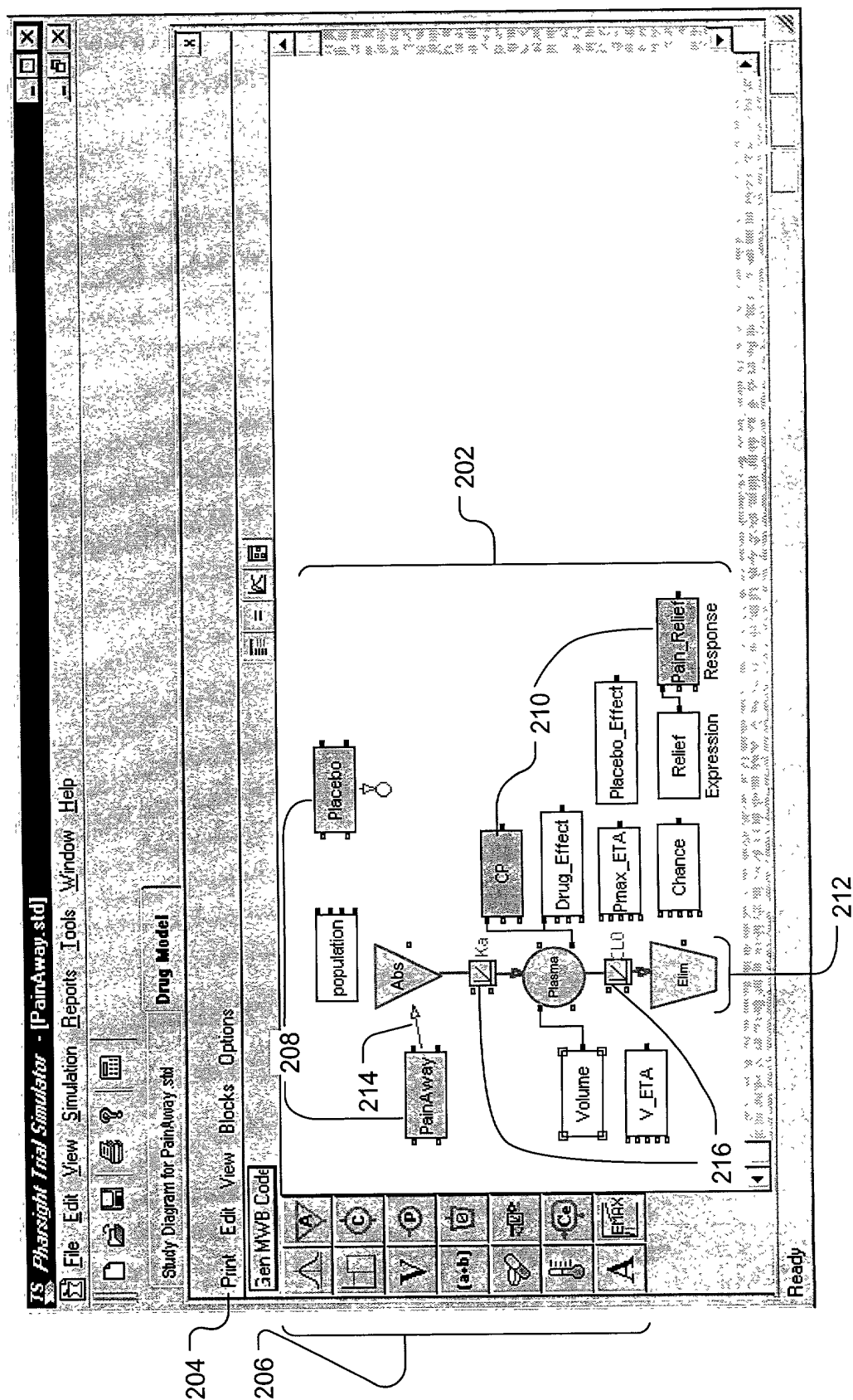
140 — CODE GENERATOR

FIG. 1

FIG. 2A

250

Block Properties ⊠

Population: population ▼

Covariates | Distributions | Continuous

Put covariates into joint distributions,
by clicking to include/exclude :

	BodyWeight	Gender	Age	eatinineClearan

252

Distribution : BodyWeight — 258

| Edit | X | | | |

Distribution : Gender

254

| Edit | | X | | |

Distribution : Age — 256

| Edit | | | X | |

Distribution : CreatinineClearance

| Edit | | | | X |

Comment:

260

Block Properties ⊠

Population: population ▼

Covariates | Distributions | Continuous

Put covariates into joint distributions,
by clicking to include/exclude :

	BodyWeight	Gender	Age	eatinineClearan

262

Distribution : BodyWeight X Age

| Edit | X | | X | |

Distribution : Gender

| Edit | | X | | |

Distribution : CreatinineClearance

| Edit | | | | X |

Comment:

☐ Show block type?

FIG. 2B
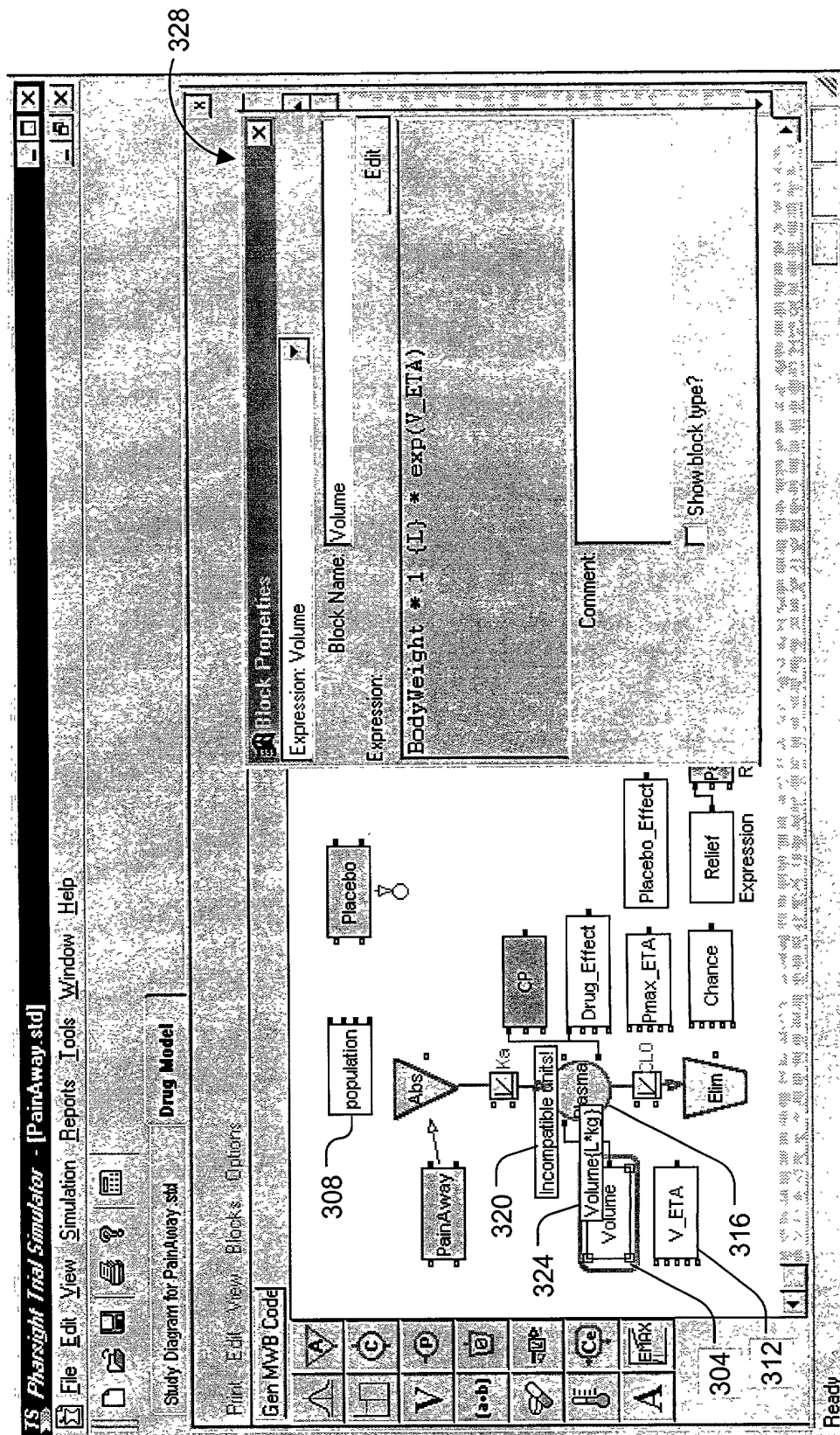
FIG. 3

402   404

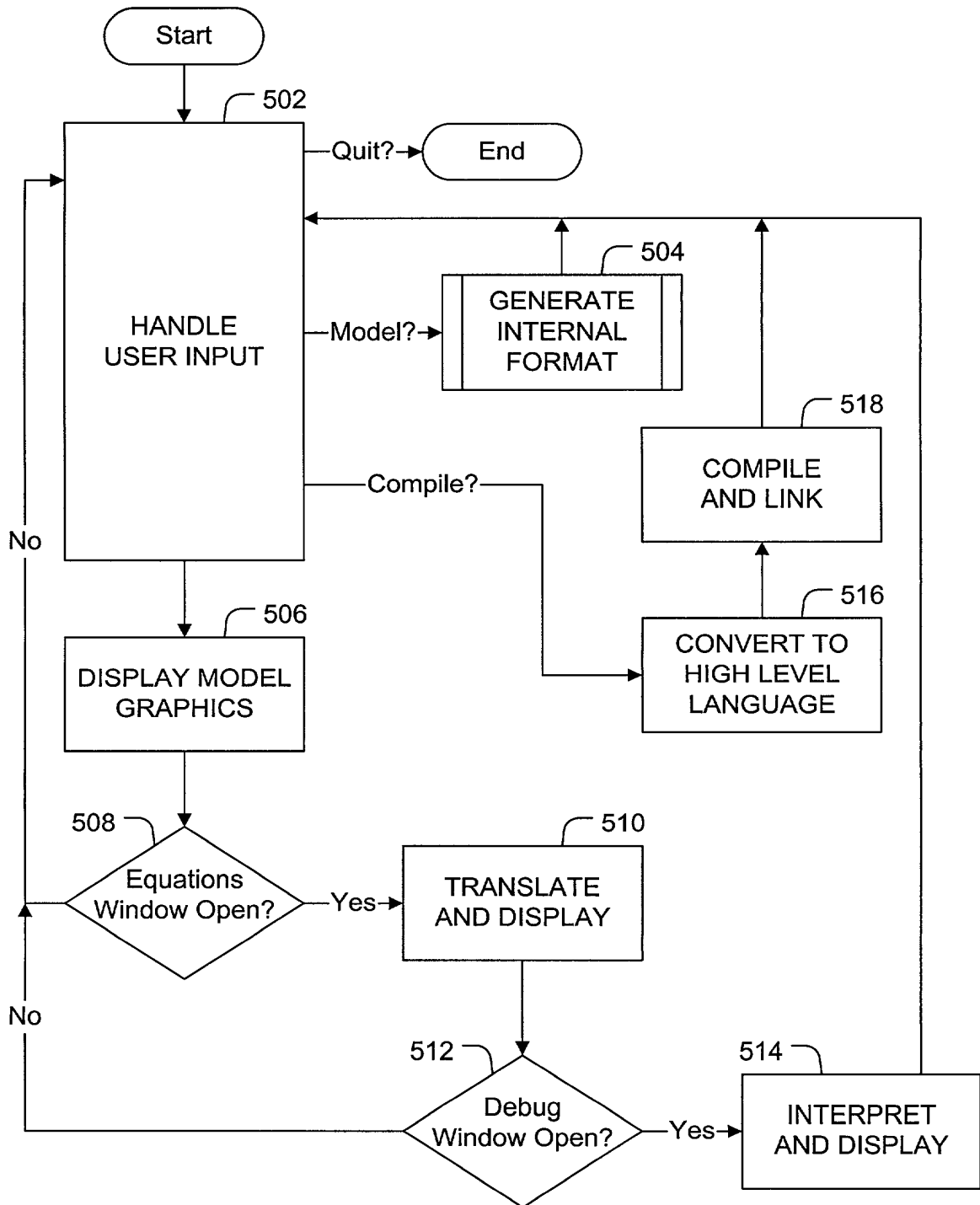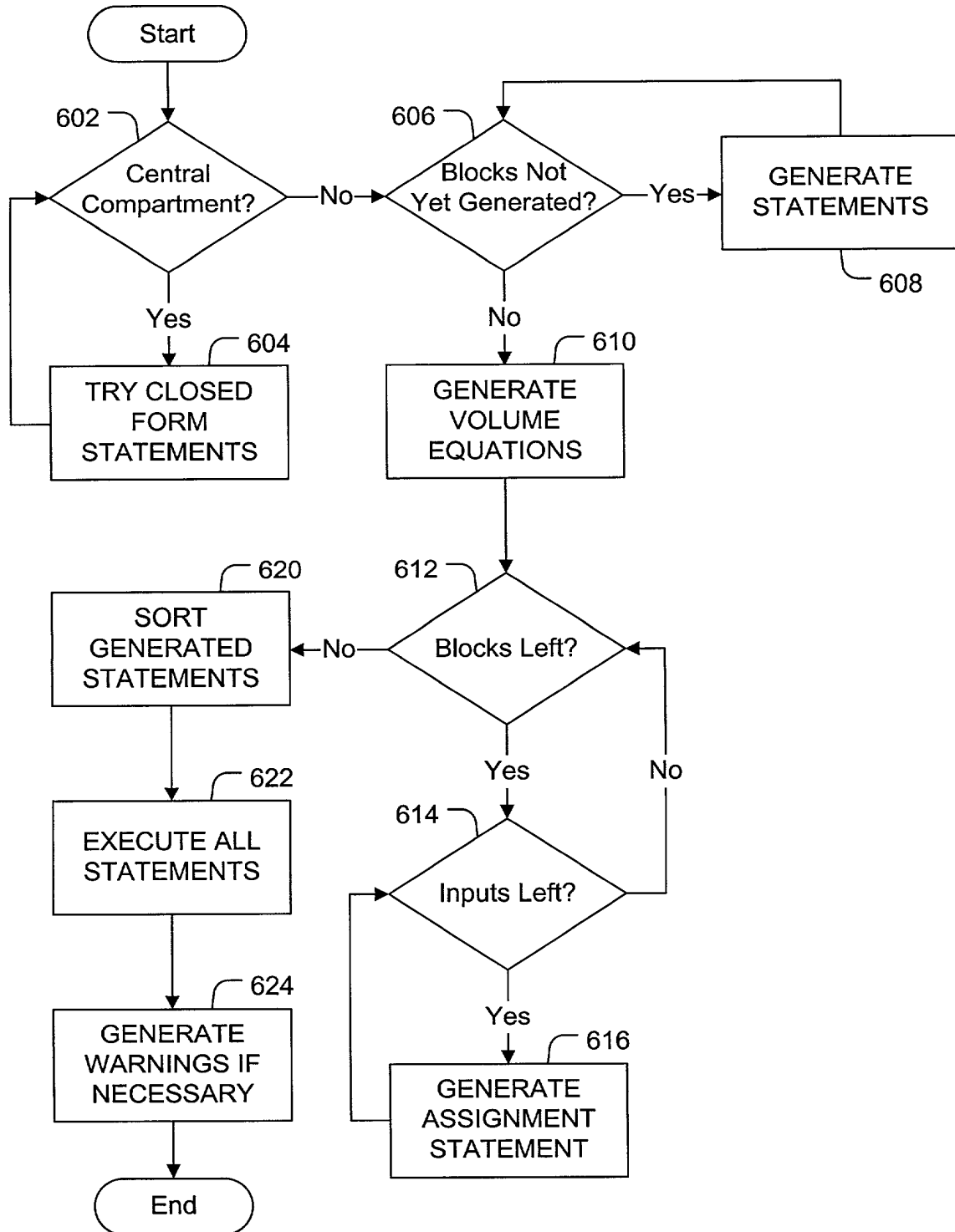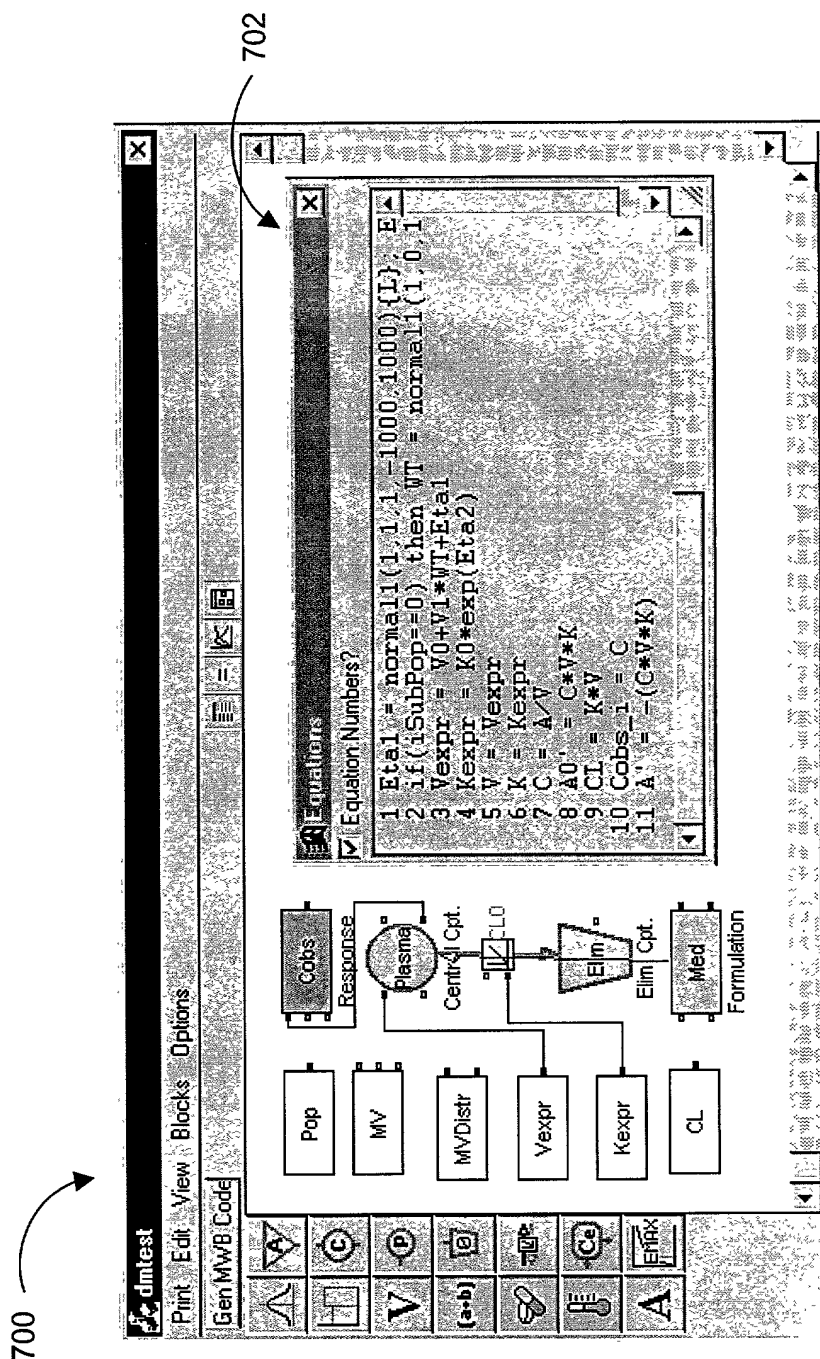|	
Const	a numeric constant
NamedConst	a numeric constant having a name, such as Male or Female
StrConst	a string constant such as 'this is a string'
Unit	a basic unit such as L(liters) or d(days)
GetPort	a reference to the value of a variable
Trinop	trinary operator, such as the conditional operator
Binop	binary operator, such as +, -, *, /, comparison, etc.
Unop	unary operator, such as unary minus, and logical .not.
TimesUnit	multiplication by a unit phrase
UnitBinop	binary unit operator, such as *, /
UnitPhrase	encapsulates a unit phrase
DelayFunc	the delay function. It's output equals its input delayed by an offset.
TableFunc	the tabular function.
Funcall	calls one of a set of built-in functions, such as sqrt, exp, ln, etc.
SetPort	stores a value into a variable
SetDerv	sets the derivative (rate of change) of a variable
DEvent	represents the action to be performed when an event fires.
CDistr	represents a univariate continuous distribution.
DDistr	represents a univariate categorical distribution.
DLogit	represents a categorical distribution determined by an input value, some offset values, and a link function.
Choose	represents block equivalent of the trinary conditional expression.
Subrcall	represents a call to an external user-written subroutine.
NewStmtSequence	represents a sequence of statements
StmtIfThenElse	represents an if-then-else statement
InitCF	initializes a closed form machine by setting its initial parameters.
Add1stOrdCF	modifies a closed form machine by convolving its parameters with a first order delay.
Add1stOrdInputCF	modifies a closed form machine by convolving its parameters with a first order delay.
CloneCF	copies one closed form machine into another.
GetValCF	reads the value of a closed form machine
AddDoseCF	adds a bolus dose to a closed form machine
AddRateCF	adds to the infusion rate in a closed form machine
IfLevel	a special if statement used to guard statements, causing them to only be executed at the proper distribution level, such as continuous, event, periodic, etc.
SetDiscrete	used to set a group of categorical variables that are jointly distributed.
DSwitch	used to choose among a set of continuous values on the basis of a set of discrete values.
MCorDistr	represents a multivariate continuous distribution with correlation matrix
MVarDistr	represents a multivariate continuous distribution with variance-covariance matrix.
MVarImport	represents a set of variables that are being imported.

FIG. 4

FIG. 5

Start

602 — Central Compartment?

No → 606 — Blocks Not Yet Generated?

Yes → GENERATE STATEMENTS 608

Yes ↓

604 TRY CLOSED FORM STATEMENTS

No ↓

610 GENERATE VOLUME EQUATIONS

620 SORT GENERATED STATEMENTS

←No— 612 Blocks Left?

Yes ↓

614 Inputs Left?

No

622 EXECUTE ALL STATEMENTS

Yes ↓

616 GENERATE ASSIGNMENT STATEMENT

624 GENERATE WARNINGS IF NECESSARY

End

FIG. 6

FIG. 7A

730

Equations

☑ Equation Numbers?

```
1  if(iSubPop==0) then switch(SetDiscrete1(ddistr(2, 0.51, 0.49), Gender, 2), BodyWeight = no...
2  A = -(A*Ka)
3  Temp_00 = normal1(1,V_ETA_mean,V_ETA_sd,V_ETA_lo,V_ETA_hi)
4  V_ETA = V_ETA_mult*Temp_00
5  Volume = BodyWeight*1(L/kg)
6  Temp_01 = normal1(1,Pmax_ETA_mean,Pmax_ETA_sd,Pmax_ETA_lo,Pmax_ETA_hi)
7  Pmax_ETA = Pmax_ETA_mult*Temp_01
8  Placebo_Effect = 0.3
9  Temp_02 = uniform(1,Chance_lo,Chance_hi)
10 Chance = Chance_mult*Temp_02
11 Relief = 1
12 V = Volume
13 Pain_Relief_i = Relief
14 C = A1/V
15 A0' = C*Cl
16 CP_1 = C
17 Drug_Effect_C = C
18 A1' = A*Ka-C*Cl
19 Drug_Effect = Drug_Effect_Emax*Drug_Effect_C**Drug_Effect_Hill/(Drug_Effect_Hill/(Drug_Effect_EC50**Drug_Ef
```
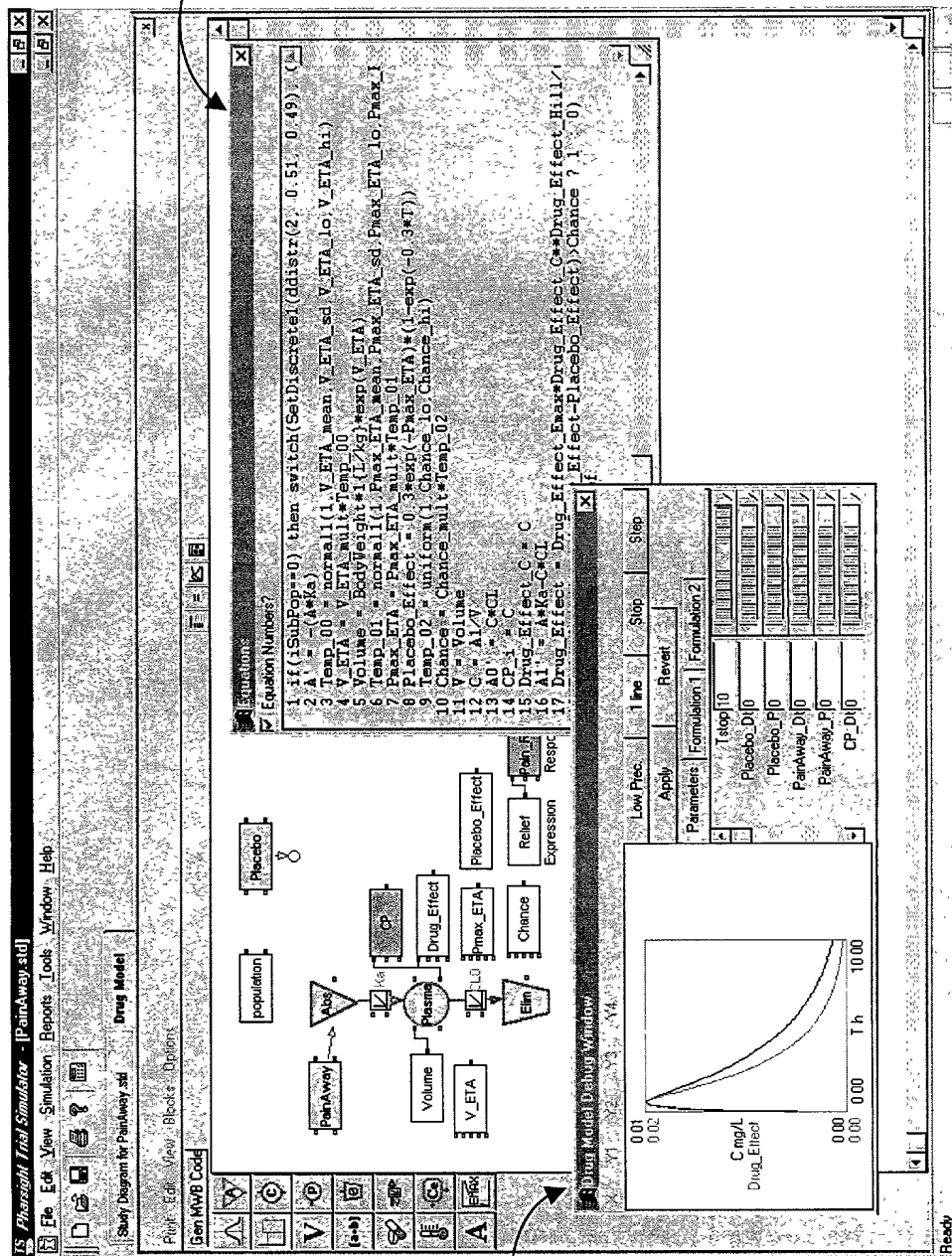
734

732

FIG. 7B

FIG. 7C

200

730

740

FIG. 7D

800

802

Processor

804

Main Memory

806

Communications Bus

Hard Disk Drive

808

810

Removable
Storage Drive

812

Removable
Storage Unit

814

Interface

Removable
Storage Unit

822

820

Communication
Interface

826

828

824

FIG. 8